

Outcome of Surgical Management of Carcinoma of the Pancreas

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Majority of the pancreatic tumours arise from ductal epithelium and practically the term pancreatic cancer is reserved for that tumour. Males are predominantly the victims with male to female ratio of 3:1 in this study. A number of etiological factors have been blamed to be associated but smoking and diabetes mellitus are closely related. Fifty percent patients in this study were found to be either current smokers or have been smoking till last five years. The tumour is notorious for its silent growth and non specific presentation. The most common symptom being jaundice when the tumour arises from head region of the gland, associated with anorexia, vomiting weight loss and malaise. Migrating thrombophlebitis is another unusual feature in some cases. The tumours of body and tail present as mass in the epigastrium. In the present study 90% tumours were arising from the head of the gland and 10% from the body. Cystic neoplasms are common in female patients and arise from the body and tail. Silent spread of the tumour involves the lymph nodes and peripancreatic tissues making it most of the time unresectable at the time of presentation. In the text 10% is the usual resectable rate. In our study the resectability rate was 25%. Management of the case depends upon the stage of the tumour at time of presentation. Surgical management is the best suitable with chance of curative resection of the tumour. Various modifications in pancreaticoduodenectomy have been done since the Whipple's procedure was introduced. Pylorus preserving pancreaticoduodenectomy is one such modification. Pancreatic stump is associated most of the time with complications of leakage. Although the techniques of pancreaticoduodenectomy have been improved with better pre operative evaluation, anaesthetic facilities and post operative care of the patient, the long term five year survival is still not much increased. Moreover, post operative hospital stay and complication rate is still high. Alternatively, bypass procedure especially where the disease is advanced and the tumour is not resectable, are applied. These palliative procedures are associated with short hospital stay, less post operative complications, early relief of symptoms and better quality of life. Short term survival is rather better in these patients as compared to those undergoing resection. Six months survival in our study was 66.6% as compared to 60% in resected cases. Supportive therapies including chemotherapy, radiotherapy and hormone therapy at present are not of much help.

Key words: CA pancreas, surgical management, outcome

Carcinoma of the pancreas is a disease of elderly with male predominance. It accounts for more than 90% of exocrine tumours and is characteristically aggressive lesion. At the time of diagnosis, in fewer than 10% of cases, the tumour is confined to the pancreas. Forty percent have locally advanced disease and more than 50% have distant spread. More than 95% of patients die of the disease eventually. The median length of survival is 18-20 months even after resection for cure.

The patients are treated usually when they are in terminal stage. The delay in diagnosis is the main factor and can be attributed to both the patient and physician due to vague and nonspecific symptoms.

The disease is common all over the world. It is the eighth most commonly occurring cancer in U.K. and the fourth and fifth leading cause of cancer death in men and women respectively in United States. We have plenty of cases in Pakistan and many surgeons are working on their own with special interest in pancreatic surgery. A little effort has been made on the subject. Comprehensive data about the disease is still awaited.

Aims and objectives:

Most pancreatic tumours arise in the head region of the gland with approximately one fourth in the region of body and tail. The tumours of the head region are associated

usually with symptoms of jaundice or gastric outlet obstruction, but that of body and tail may be associated only with gastric outlet obstruction. The tumours of body and tail usually present late when they are big enough to appear as a mass in the epigastrium. One purpose of this study was to determine different sites of origin of such tumours from the gland. The other one was to assess how many of the tumours of the gland are resectable at the time of presentation. In addition, it was intended to make a comparison between resectable and unresectable (but surgically managed) tumours, regarding post operative complications and course of the disease. In the end to establish which treatment (under different situations) is suitable for the patient.

Patients and methods:

It was a prospective study of pancreatic cancer patients coming to Lahore General Hospital, Lahore over a period of two years, i.e. from September 2003 to September 2005. Initially it was planned for a study of fifteen cases but extended to twenty on availability of more cases. The patients were collected for study at random from all the three general surgery units of the hospital, admitted through Outpatient Department or Casualty. There were fifteen male and five female patients with age ranging from 32-76 years. Detailed clinical history with major

presenting complaints and examination was done supported by routine laboratory tests, abdominal ultrasound examination, ERCP and CT scan when available was done.

Exploratory laparotomy (through mid line incision) was carried out in most cases. Operative findings as tumour size and involvement of extrapancreatic tissue were noted. Surgical resection was performed whenever it was technically possible and tumour was resectable with no distant metastases. Unresectable tumours were those with extensive local invasion of major visceral vessels as superior mesenteric artery, portal vein, or hepatic artery and peripancreatic tissue. Diagnosis was confirmed histologically. Pancreatic endocrine tumours, cancer of bile duct, duodenum or ampulla of Vater were excluded from the study.

In resectable cases classical Whipple's procedure with resection of distal stomach was performed. In unresectable cases bypass procedure as cholecystojejunostomy, choledochojejunostomy, gastrojejunostomy and jejunojejunostomy were performed. No patient was treated with adjuvant radiotherapy or chemotherapy.

Post operative complications in both groups were noted. Pancreatic leakage was diagnosed if significant amount of amylase rich fluid came out through drains.

Post operative hospital stay period and hospital mortality was compared for both groups. Patients were followed up for six months post operatively. Follow up included clinical evaluation, routine laboratory tests one month after operation, abdominal ultrasound and x-rays chest after three months or when indicate. Survival of the patients was determined by OPD visits, personal letters and telephone contact.

Percentage resectability of the tumour and outcome as post operative complications mortality and six months survival in both resectable and unresectable groups were compared.

Results:

During the study period of two years at Lahore General Hospital, Lahore twenty cases of proven pancreatic cancer were collected at random. There were fifteen male (75%) and five female (25%) patients, both with mean age group of 53 years ranging from 32-76 years (Table 1). Fifty percent patient (n=10) were smokers or had been smoking till last five years. Three patients (15%) were diabetic. One was known and two were diagnosed on routine investigations at admission.

The patients presented mostly with combination of symptoms. Major complaints were jaundice n=18 (90%), the pain n=10 (50%) consisted of abdominal pain n=7 (35%) and back pain n=3 (15%) anorexia n=4 (20%), vomiting n=3 (15%), itching n=3 (15%), weight loss n=3 (15%), fever n=2 (10%), malaise n=2 (10%), and migrating thrombophlebitis n=1 (5%).

The patients were divided in two groups according to resectability of the tumour. Out of total (n=20), five were resectable. Classic Whipple's procedure n=5 (25%) with resection of distal stomach was performed. Twenty percent of the patients undergoing Whipple's procedure were female. Mean age of the patients undergoing Whipple's procedure was 46 years with range from 32-60 years.

Surgical palliative procedure were performed on other patients n=15 (75%) including 26.7% of female patients. The mean age in this group was 55.6 years with range from 42-76 years. Palliative procedures performed were cholecystojejunostomy n=6 (40%), cholecystojejunostomy and gastrojejunostomy n=3 (20%), choledochojejunostomy only n=2 (13.3%), choledochojejunostomy with gastrojejunostomy n=3 (20%), gastrojejunostomy only n=1 (6.7%), and enteroenterostomy associated with either cholecystojejunostomy or choledochojejunostomy n=5 (33.3%) (Table 2).

Table 1: Age distribution in relation to number of patients and procedure

10 years Distribution	=n	Procedure	
		Whipple	Palliative
30-40 years	2	2	0
41-50 years	9	2	7
51-60 years	5	1	4
61-70 years	3	0	3
71-80 years	1	0	1

The mean duration of procedure was 3:15 hours (2:15-4:30) in case of pancreaticoduodenectomy procedure and 1:45 hours (2:10-35) in case of palliative procedure (Table 4).

The head of the gland was the predominant tumour site n=18 (90%) in both cases with involvement of neck n=4 (20%) and periampullary area n=2 (10%). The origin from body n=2 was in two cases (Table 5).

Mean tumour size in resected cases was 2.6cmx3.7cm, while in patients who underwent palliative procedure was 5.2cmx6.2cm.

Seventy percent of the tumours n=14 were well differentiated, 20% moderately differentiated n=4 and 10% were poorly differentiated n=2.

Sixty five percent of the cases n=13 showed peri pancreatic tissue involvement 30% of the cases n=6 showed involvement of para aortic lymph nodes, 25% (n=5) coeliac lymph nodes, and 10% (n=2) mesenteric lymph nodes. Hepatic artery (n=2) was involved in 10%, portal vein (n=2) 10%, liver (n=1) 5%, duodenum (n=6) 30%, transverse mesocolon (n=3) 15%, and extrapancreatic neural plexus (n=2) 10%. In one case, although no peripancreatic involvement was present yet two osteolytic lesions confirmed on bone scan were present.

Major post operative complications were registered in 30% of patients (n=6). In resectable cases the complication rate was 40% (n=2), whereas in palliative

cases it was (26.6%) (n=4). The most frequent complication in resectable cases was pancreatic leakage (n=2) 40%. Delayed gastric emptying was the second most common (n=1) 20%.

Table 2

Procedure	(n=)	%age
Cholecystojejunostomy	6	40
Cholecystojejunostomy with gastrojejunostomy	3	20
Choledochojejunostomy	2	13.3
Choledochojejunostomy with gastrojejunostomy	3	20
Gastrojejunostomy alone	1	6.7
Enteroenterostomy*	5	33.3

*Additional procedure either with cholecystojejunostomy or choledochojejunostomy.

Table 3: Operation data: comparison between Whipple's procedure and surgical palliative procedure

Subject	Whipple's	Palliation
Number of patients	5	15
Average tumour size	2.6cm 3.7cm	5.2cm -6.2cm
Average duration of procedure	3 hrs 15 min	1hr 45 min
Post operative hospital stay	(14-30 days) Average 22.6	(9-26 days) Average 15.3

Table 4: Different sites of tumour origin

Sites	(n=)	%age
Head	n=18	90
Body	n=2	10

In the palliative group, bile leakage (n=2) 13.3% and gastrointestinal bleeding (n=2) 13.3% were common. Other complications were cholangitis (n=1) 6.7% and delayed gastric emptying (n=1) 6.7%. The complication common to both groups was delayed gastric emptying (n=2) 10%.

Sixty percent of cases in resectable group (n=3) and 73.3% of cases in unresectable group (n=11) were free of complications.

The mean length of post operative hospital stay after pancreaticoduodenectomy was 22.6 days (14-30 days) which was significantly longer than the post operative stay in non resected but managed palliative group i.e. 15.3 days (range 9-26 days).

Thirty days hospital mortality was 20% in resectable group (n=1) and 13.3% in palliative group (n=2). After six months, re-evaluation of the cases showed 60% survival in resectable (n=3) group and 66.6% survival in palliative group (n=10).

Table 5: Historical differentiation of Adenocarcinoma of Pancreas

Types	=n	%age
Well differentiated	14	70
Moderately differentiated	4	20
Poorly differentiated	2	10

Table 6: Extra pancreatic involvement of different tissues

Structure/tissue involved	=n	%age
Para-aortic lymph	6	30
Coeliac lymph nodee	5	25
Mesenteric lymph node	2	10
Hepatic artery	2	10
Portal vein	2	10
Liver	1	5
Duodenum	6	30
Transverse mesocolon	3	15
Extrapancreatis	2	10
Total cases with Involvement	13	65

Table 7: Common Post Operative Complications

Complication	Procedure	%age
Pancreatic leakage	Whipple's	40
Delayed gastric emptying	Whipple's	20
Bile leakage	Palliation	6.7
G.I. Bleeding	Palliation	13.3
Cholangitis	Palliation	6.7

Discussion:

Adenocarcinoma of the pancreas is a disease of elderly, with male predominance. Due to nonspecific symptoms, most patients present for treatment late when the disease has already spread. This late presentation is a major factor that influences resectability.

It is the fifth leading cause of cancer death in United States. In literature the resectability rate of the tumour in the region of head of the gland is reported between 15-20%^{1,2}. Calculated resectability rate of 25% in this study is higher than previously reported. the reason could simply be due to less number of total patients and random selection of the cases. Common reasons for non-resectability are local invasion into the peripancreatic tissue, the root of mesentry or the celiac axis. In our 75% unresectable patients, 65% showed peripancreatic involvement. Hepatic artery and portal vein were involved in 10% cases each. Among the lymph nodes, para-aortic group (30%) was mainly involved (Table 6).

It is widely accepted that surgical resection provides the only chance for long term survival. However reported thirty days mortality rate for this procedure is 25%. Other recent surveys in U.S. Veterans Administration Hospital System³ and French Association of Surgery⁴ still report mortality rates of 6%-10%. It was 20% in our study. By the 1970s, the high operative mortality and morbidity and poor long term survival led some surgeons to suggest that Whipple's procedure should be abandoned. Crile concluded that pancreatic cancer was incurable by pancreaticoduodenectomy and just biliary bypass should be performed as palliation. Shaprio (1975)^{5,6} in a comparison of pancreaticoduodenectomy and palliation by biliary bypass with twenty four patients each concluded that mean survival was similar with no long term survivors in either case.

In the present study all the patients were not followed for long time but six months follow up showed survival

rate of 60% in case of Whipple's procedure and 66.6% in case of palliative bypass procedure.

At the same time major advances in the palliation of pancreatic cancer have been made in recent years. Palliative procedures should have low mortality and morbidity, provide good quality of life with minimal hospitalization. Non-operative palliation of obstructive jaundice can be accomplished endoscopically or percutaneously in more than 90% patients⁷. However only surgical palliation offers the opportunity to control all the major symptoms as biliary obstruction can be managed with cholecystojejunostomy, choledochojejunostomy or hepaticojejunostomy. Similarly duodenal obstruction can be managed with gastrojejunostomy and management of pain can be improved with use of intraoperative chemical splanchnicectomy with alcohol. Some researchers⁸ have concluded that there is no role of prophylactic gastroenteric bypass in patients without symptoms of gastric obstruction and the procedure be performed later on when indicated. Despite widely patent anastomosis, delayed gastric emptying has been reported in 14-26% patients post operatively. Arguments in favour of gastric bypass accompanied with biliary bypass as an initial procedure are that:

1. it does not increase morbidity and mortality
2. it rather decreases the need for reoperation associated with operative mortality of 25%⁹.

In biliary bypass, choledochoenterostomy is technically more demanding procedure, considered favourably, but this procedure did not yield results significantly superior to those of cholecystoenterostomy. In our study, biliary bypass was done in 93.3% patients undergoing palliation, and gastric bypass in 46.7% of patients with success rate of 85.5% and 71.5% respectively. Minor biliary leakage and gastrointestinal bleed was managed conservatively.

Biliary obstruction was bypassed as cholecystojejunostomy (n=9) and choledochojejunostomy (n=5). Two cases of biliary leakage, one in each group were noted postoperatively. Therefore success rate was 88.9% in case of cholecystojejunostomy and 80% in case of choledochojejunostomy. Therefore cholecystojejunostomy with easy access is a better option. Total post operative complication rate for palliative procedure (26.6%) was far less than Whipple's procedure (40%). Pancreatic fistula was the most common post operative complication followed by delayed gastric emptying. Studies show earlier liquid phase recovery than prolonged solid phase¹⁰. The management of pancreatic fistula includes adequate external drainage with maintenance of fluid and electrolyte balance, total parenteral nutrition and meticulous care of drainage site. Persistent fistula and uncontrolled sepsis needs exploration.

Five year survival rate in a study of 201 patients undergoing pancreaticoduodenectomy at the John Hopkins Hospital¹¹ was 21%, concluding improvement in survival

with tumour size less than 3cm in diameter and with negative nodal involvement. Cameron and associates¹² reported a 19% five year survival in a group of eighty nine patients. Tumour size more than 2cm, positive lymph nodes and vessels involvement were adverse prognostic factors. Nitecki and colleagues¹³ reviewing Mayo clinic experience reported five year survival of 6.8% after resection. Willett and colleagues¹⁴ emphasized the importance of negative pathologic margins with survival rate of 13%. It is suggested that patient characteristics and tumour findings rather than operative procedure affect long term survival after resection¹⁵. Improvement in long term survival create doubt whether the actual techniques are improving or the disease actually is attenuating as has been suggested¹⁶.

Conclusion:

Most tumours are unresectable at the time of presentation but despite this fact, surgical resection provide the only chance for survival. Pancreaticoduodenectomy appears to be associated with a somewhat longer operative time and longer post operative hospital stay and therefore, likely higher hospital costs. Long term survival after resection is very little and short term survival both in resection of the tumour and palliative bypass is not much different. Patients with unresectable tumour benefit from the palliative bypass procedures which is favoured due to relief of symptoms and better quality of life. Therefore it is the procedure of choice. The method of palliation can be tailored to the needs of the patient's estimated survival. Cholecystojejunostomy along with gastrojejunostomy is favourable due to easy access and less post operative complications, provided the gallbladder is not resected and the tumour has not extended to involve the cystic duct. Choledochojejunostomy is the next favoured. So surgical palliation is better option with less duration of hospital stay, less post operative morbidity and mortality, and better short term survival.

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